

Contains Nonbinding Recommendations
Draft Guidance on Nilotinib Hydrochloride Monohydrate

This draft guidance, once finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the Office of Generic Drugs.

Active ingredient: Nilotinib Hydrochloride Monohydrate

Form/Route: Capsules/Oral

Recommended studies: 1 study

Type of study: Fasting

Design: Single-dose, two-way, crossover *in vivo*

Strength: 200 mg

Subjects: Healthy males and nonpregnant females, general population.

Additional Comments: 1) Females should not be lactating, and if applicable, should practice abstention or contraception during the study. 2) Patients with hypokalemia, hypomagnesemia, or long QT syndrome, or a history of cardiac disease should be excluded. 3) Drugs known to prolong the QT interval should be avoided within 4 weeks prior to study. Please see <http://www.azcert.org/medical-pros/drug-lists/drug-lists.cfm> for a list of agents that prolong the QT interval. 4) Strong CYP3A4 inhibitors or inducers should be avoided within 4 weeks prior to study. Please see <http://medicine.iupui.edu/flockhart> for a list of inhibitors and/or inducers. 5) Grapefruit, pomegranate, star fruit and Seville oranges should be avoided for 7 days prior to dosing. The juices and products containing these fruits should also to be avoided. Subjects should also refrain from taking St. John's Wort. 6) Caution should be exercised if co-administered with drugs that are substrates or inhibitors of P-glycoprotein. 7) Caution should be exercised if co-administered with narrow therapeutic index drugs that are substrates of CYP3A4, CYP2B6, CYP2C8, CYP2C9, CYP2D6 or UGT1A1. 8) Subjects should have normal renal and hepatic function. 9) Males and their female partners need to practice adequate contraception for at least 1 week after the last nilotinib dose.

Analytes to measure (in appropriate biological fluid): Nilotinib in plasma.

Bioequivalence based on (90% CI): Nilotinib

Waiver request of *in-vivo* testing: Not Applicable

Dissolution test method and sampling times:

Please note that a **Dissolution Methods Database** is available to the public at the OGD website at <http://www.accessdata.fda.gov/scripts/cder/dissolution/>. Please find the dissolution information for this product at this website. Please conduct comparative dissolution testing on 12 dosage units each of all strengths of the test and reference products. Specifications will be determined upon review of the application.